

## **REMARKS**

### **I. Brief summary of amendments**

Claims 1 and 6 have been amended to delete the phrase “an aqueous solution comprising” and to recite “is an aqueous solution.” Support for an external preparation being an aqueous solution can be found throughout the application as filed. See, for example, page 7, line 24, to page 8, line 10; and Examples 1-3 in Table 1 on page 7 (wherein the components are water mixed with aqueous solutions of water soluble polymer and glycolic acid). Accordingly, no new matter has been added.

Applicant reserves the right to pursue the subject matter of any claim as previously presented in related applications, including continuing applications.

### **II. The rejections under 35 U.S.C. § 103(a) should be withdrawn.**

The Examiner rejected claims 1, 5, 8, 9 and 12 as allegedly unpatentable over Groh (U.S. Patent No. 5,863,943) in view of Tung et al. (American Journal of Clinical Dermatology, 1(2), pp. 81-88 (2000)). The Examiner also rejected claims 6, 7, 10 and 11 as allegedly unpatentable over Duffy (U.S. Patent No. 5,703,122) in view of Tung et al. ((American Journal of Clinical Dermatology, 1(2), pp. 81-88 (2000))). The Applicant respectfully requests reconsideration in view of the amendments presented herein and the following remarks.

#### **A. The combined teachings of Groh and Tung fail to disclose or suggest the invention of claims 1, 5, 8, 9, and 12.**

As explained below, the invention specified by claims 1, 5, 8, 9, and 12 is not obvious in view of, e.g., limitations relating to pH and aqueous character.

1. A composition comprising glycolic acid and PEG, wherein the pH is 2.0 or less as recited in independent claim 1, would not have been obvious.

The Examiner alleges that although Groh discloses examples with a pH of 4-6, that this does not teach away from the broader disclosure, which suggests the formulation of the composition at an appropriate pH; and a pH of 1.4 for glycolic acid compositions is taught by Tung to be useful for chemical exfoliation of the skin. The commonality of the references cited on which the Examiner relies is alleged suitability for the treatment of acne.

Groh does, in fact, teach away from the pH required in claim 1. The Examiner alleges that Groh teaches “the formulation of the composition (e.g. at an appropriate pH) for the treatment of other conditions in which glycolic acid was known to be useful (see e.g. column 1, lines 37-39) . . . .” However, Groh column 1, lines 37-39, discusses a particular **difficulty** with alpha hydroxyl acid oil-in-water emulsions: stabilization. Groh teaches that stabilization of these preparations has been difficult due, in part, to the acidic nature of the preparation, their instability, their relatively short shelf life and tendency to develop an aesthetically unpleasant character. Groh goes on in column 1, at lines 37-40, to teach that in order to achieve the best possible skin treatment (treatment can broadly encompass addressing specific skin disorders, moisturizing, de-keratinization, etc.) it is desirable to provide a preparation, such as a lotion or crème, which is resistant to being washed off upon rinsing of the skin. Therefore, it is an object of Groh to provide a skin conditioning treatment, an oil-in-water emulsion which is stable, aesthetically pleasing and a suitable carrier for one or more alpha hydroxyl acids.

Groh teaches the “Inventive Composition % (wt/wt)” in Table 1. Near the end of Table 1, Groh lists the initial pH for the inventive composition which range from 3.62 to 3.70. Groh further describes the inventive composition in column 7, lines 15-23:

The composition described is gentle, notwithstanding the use of cationic surfactants, and of **acidic pH (approximately 4.0-6.0)**, suppressing any “amine” smell and **consistent with natural skin pH. It is thus suitable for application to any portion or portions of human skin . . .**” (Emphasis added)

Thus, the Examiner's characterization of Groh's disclosure as "broader" than the disclosed example is incorrect, at least with respect to pH. In describing a pH range of 4.0-6.0, Groh was not merely describing an example or an embodiment of the invention; Groh was describing Groh's "Inventive Composition" itself. Groh does teach a preparation "at an appropriate pH," but that pH must be viewed in light of what *Groh* teaches is "appropriate" with respect to pH. One of ordinary skill would have looked to the objectives of Groh's invention, as described by Groh, and would have recognized that a pH range of 4.0-6.0 was the "appropriate pH." Further, one of ordinary skill in the art who read Groh would not have been motivated to adjust the pH of Groh to 1.4, because a pH of 1.4 is not "gentle" or "suitable for application to any portion or portions of human skin" as taught by Groh. Thus, Groh's teachings with respect to pH are indeed a teaching away from the pH used in the present invention.

Moreover, the Examiner's allegation that one would ignore Groh's teachings about a mild pH in view of Tung does not withstand scrutiny for additional reasons already of record. The Examiner's alleged motivation for combining these two documents related to *treatment of acne*. Tung does NOT teach Tung's low pH for treating acne. Rather, Tung teaches that a pH of 3.8 is efficacious for acne. (See page 86, right column, last paragraph: "... partially neutralized to a pH of 3.8 are efficacious and have a low irritation rate in these groups of patients ...") Tung's pH of 3.8 for acne is within 0.2 pH units of Groh's range of 4.0 to 6.0. Thus, if one of ordinary skill would have tried to combine the two documents to arrive at a treatment for acne, one would have chosen Groh's pH (4.0 to 6.0) or modified it only slightly, down to Tung's proposed pH of 3.8. It would not have been obvious, based on the combined teachings of these documents, to select the much more acidic pH recited in the present claims.

To summarize, the pH element of the claims would have been unobvious. With respect to the element of pH, the rejection is premised on the idea that it would have been obvious to combine these documents to develop an improved treatment for acne **but** go **against** Groh's fundamental teachings about mild pH suitable for any portion of the skin, and go **against** both Groh's and Tung's teachings about pH for an acne composition when combining the two documents. There is no basis for this conclusion, except improper hindsight.

2. A composition comprising glycolic acid and PEG, wherein the preparation is an aqueous solution as recited in independent claim 1, would not have been obvious.

The Examiner also alleges that Groh teaches a composition comprising an aqueous solution comprising water, glycolic acid and PEG. The Examiner notes that the open language of claim 1 (as previously presented) allows for additional components in the external preparation (e.g., an oil phase). Even if (for the sake of argument) this analysis is accepted on its face, it no longer applies to the amended claims. Applicant has amended claims 1 and 6 to recite a composition comprising glycolic acid and PEG, wherein the preparation **is** an aqueous solution. Thus, the amended claim is not permissive of a substantial oil phase because a composition with a substantial oil phase is not an aqueous solution. Groh discloses an *emulsion* comprising non-aqueous moisturizing components: "The essential elements that constitute the delivery system for the AHA are water and an oil phase to form the basic emulsion ...." (See and column 2, lines 24-26; see also the abstract and claim 1 of Groh.) An emulsion as described in the cited reference is not an aqueous solution as required by the amended claims. Thus, the inventions of Groh and of claim 1 are clearly different.

The teachings in the Tung document do not disclose or suggest modifying the Groh composition to, e.g., remove oleaginous components and change the character of the composition from an emulsion to an aqueous solution. Groh does not disclose or suggest an aqueous solution nor does Groh mention one of the problems to be solved in the present invention: the difficulty in uniform application and absorption of an aqueous solution. Therefore, an aqueous solution would not have been obvious from Groh.

For all of these reasons, the rejection of claim 1 and those claims dependent thereon under 35 U.S.C. § 103(a) should be withdrawn.

**B. The combined teachings of Duffy and Tung fail to disclose or suggest a composition comprising glycolic acid and polyvinyl alcohol wherein the preparation is an aqueous solution as recited in independent claim 6.**

The Examiner alleges that Duffy teaches an aqueous composition comprising alpha hydroxyl acid, glycolic acid, polyvinyl alcohol and water, but does not explicitly teach the composition having a pH of 1.4 or less. The Examiner alleges that Tung teaches glycolic acid peel products having a pH of 1.4 or less and a method of chemically peeling the skin. The Examiner argues that it would have been obvious to one of ordinary skill to prepare the composition of Duffy at a pH of 1.4 or less and to practice a method of chemically peeling the skin, since this pH was known to be appropriate for chemical peel procedures and the composition of Duffy was known to be useful in the treatment of conditions which glycolic acid is known to treat.

The Applicant respectfully disagrees. First, Duffy does not disclose a preparation comprising glycolic acid and polyvinyl alcohol wherein the preparation is an aqueous solution as recited in amended claim 6. Duffy recites polyvinyl alcohol in claims 2 and 11 as one of several vehicles for the preparation, including water. Duffy teaches a composition comprising an active ingredient such as glycolic acid (see Example 1), ascorbic acid and a pharmaceutically acceptable vehicle (see claim 1). Duffy further teaches that the vehicle component of the preparation may be water, alcohol, propylene glycol or glycerin (column 4, lines 63-65 and claim 2).

Second, Duffy teaches compositions with a pH of 2.4, 3.7, 3.8, 3.9 and 5.08 (columns 6 and 7, Example 1). The central purpose of Duffy is to reduce skin irritation resulting from skin treatment. Example 1 teaches a preparation of glycolic acid and ascorbic acid with a pH of 2.4 (composition B). Duffy tested the compositions twice daily on 20 subjects for seven days and recorded their irritation responses. A similar study was done in Example 2 using partially neutralized glycolic acid. Compositions A-C in Examples 1 and 2 were tested for irritation response in subjects. The lowest pH demonstrated without the addition of ascorbic acid was 2.4 (composition A) and 3.9 (composition D) both of which

demonstrated Type 3 responses (column 6, lines 54-62 and column 7, lines 26-29). Type 3 responses are characterized by numerous, tiny pinpoint bumps covering the treatment site, papules and/or pustules as well as severe itching which does not dissipate. Type 3 responses are classified as a “significant reactions” (column 6, lines 13-24). The ascorbic acid containing counterparts of compositions A and D, compositions B and F showed significant reduction in Type 3 irritation response.

Duffy describes the results of these Examples as “clearly show[ing] that ascorbic acid is unexpectedly useful in preventing irritation caused by topically applied active ingredients.” (column 7, lines 51-53).

One of ordinary skill would not have been motivated to reduce the pH of Duffy’s compositions to the pH taught in Tung of 1.4. A reduction in pH of Duffy’s compounds to 1.4 would have been expected to drastically increase the irritation response reported by subjects in Examples 1 and 2. It would, therefore, have defeated Duffy’s purposes to prepare the mixture of Duffy at the pH of Tung (0.1-1.4).

Thus, it would not have been obvious to one of ordinary skill to try to combine Tung and Duffy because it would not have been obvious to modify Duffy in a manner that defeats a central purpose of Duffy. Even if one were to have attempted to combine the teachings, one would still have followed the central tenet of Duffy that the compositions should contain ascorbic acid at a pH between 2.4 and 5.08 to reduce skin irritation, with knowledge that pH as low as 2.4 caused undesirable “Type 3” responses. Because Duffy teaches away from claim 6, a preparation comprising glycolic acid and polyvinyl alcohol wherein the preparation is an aqueous solution of pH 2.0 or less, it would have been unobvious to combine the teachings of Duffy and Tung to arrive at the claimed invention.

For all of these reasons, the rejection of claim 6 and those claims dependent thereon under 35 U.S.C. § 103(a) should be withdrawn.

### **III. Conclusion**

No fees are believed to be due with the filing of this paper. However, the Director is authorized to charge any additional fees deemed necessary to Deposit Account No. 13-2855, under order number 19036/40139. If the Examiner believes that a telephone conversation would expedite allowance of the claims, he is invited to contact the undersigned at the number below.

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Respectfully submitted,

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